SUPPLEMENT ARTICLE

Breast-Feeding Decreases the Risk of Sporadic Salmonellosis among Infants in FoodNet Sites

Samantha Y. Rowe,[1,a] Jocelyne R. Rocourt,[1,a] Beletshachew Shiferaw,[4] Heidi D. Kassenborg,[5] Suzanne D. Segler,[3] Ruthanne Marcus,[6] Pamala J. Daily,[7] Felicia P. Hardnett,[2] and Laurence Slutsker,[1,a] for the Emerging Infections Program FoodNet Working Group[b]

[1]Foodborne and Diarrheal Diseases Branch and [2]Biostatistics and Information Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, [3]Georgia Emerging Infections Program, Atlanta; [4]Oregon Health Division, Portland; [5]Minnesota Department of Health, Minneapolis; [6]Connecticut Emerging Infections Program, New Haven; and [7]California Emerging Infections Program, Berkeley

Among the population of the Foodborne Diseases Active Surveillance Network (FoodNet) surveillance areas ("FoodNet sites") in 1996, children under 12 months of age had the highest incidence of sporadic salmonellosis. We conducted a case-control study in 5 FoodNet sites to identify risk factors for sporadic infant salmonellosis. A case patient was a child under 12 months of age with a laboratory-confirmed, nontyphoidal serogroup B or D *Salmonella* infection. Twenty-two case patients were matched with 39 control subjects by age and either telephone exchange or vital record birth list. In a multivariate analysis, case patients were more likely to have a liquid diet containing no breast milk than a liquid diet containing only breast milk (matched odds ratio, 44.5; $P = .04$). Case-patients were more likely to reside in a household where a member had diarrhea (matched odds ratio, 13.2; $P = .01$). To decrease their infants' risk of salmonellosis, mothers should be encouraged to breast-feed their infants. Caretakers of infants should learn about salmonellosis, hand washing, and safe preparation of formula and solid food.

Each year in the United States, >1.4 million persons become infected with nontyphoidal *Salmonella*, and almost 600 persons die as a result of this illness [1]. In 1998, the estimated annual costs of medical care and lost productivity due to foodborne *Salmonella* infections ranged from $0.5 billion to $2.3 billion [2]. Most *Salmonella* infections cause mild-to-moderate gastroenteritis [3], but severe infections, including bacteremia and meningitis, also occur. Groups at higher risk of severe illness and death from *Salmonella* infection are infants, elderly persons, and persons with impaired immune systems [4]. In particular, invasive disease and death from *Salmonella* infection occur more frequently among infants than among older children [5].

In 1996, data from the Foodborne Diseases Active Surveillance Network (FoodNet) revealed differences between age groups in the incidence rate of nontyphoidal *Salmonella* infection. The overall annual incidence of nontyphoidal *Salmonella* infection was 14.5 cases per 100,000 population; the highest age-specific incidence was among children <12 months old (141.6 cases per 100,000 infants) [6]. Furthermore, of all culture-confirmed *Salmonella* infections, 13.2% occurred in children <12 months old [6].

Although salmonellosis among adults and older children has been associated with consumption of contam-

Financial support: Centers for Disease Control and Prevention's National Center for Infectious Diseases, US Department of Agriculture Food Safety and Inspection Service, and Food and Drug Administration Center for Food Safety and Applied Nutrition.

[a] Present affiliations: Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, Georgia (S.Y.R.); Food Safety Program, World Health Organization, Geneva, Switzerland (J.R.R.); and Malaria Branch, Division of Parasitic Diseases, Nation Center for Infectious Diseases, Centers for Disease Control and Prevention/Kenyan Medical Research Institute, Kisumu, Kenya (L.S.).

[b] Working group members are listed at the end of the text.

Reprints or correspondence: Samantha Rowe, Rollins School of Public Health, Dept. of Epidemiology, 4th Fl., 1518 Clifton Rd. NE, Atlanta, GA 30322 (syang06@sph.emory.edu).

Clinical Infectious Diseases 2004; 38(Suppl 3):S262–70

1058-4838/2004/3808S3-0020

inated food, contact with pets or domestic animals, or recent foreign travel [7–11], risk factors for salmonellosis among infants are less clear. Studies that include infants have suggested that breast-feeding is associated with a decreased risk of salmonellosis [12–15]. However, studies have failed to show associations between infant salmonellosis and risk factors described for adults and older children [13, 16–18]. Therefore, we conducted a population-based case-control study to determine risk and protective factors for sporadic salmonellosis among infants living in the FoodNet surveillance areas (also known as "FoodNet sites").

METHODS

Active surveillance. The study was conducted for a 12-month period in 1996 and 1997 in 5 FoodNet sites: Minnesota, Oregon, and selected counties in California (Alameda and San Francisco), Connecticut (Hartford and New Haven), and Georgia (Cobb, Clayton, Douglas, DeKalb, Fulton, Gwinnett, Rockdale, and Newton). In 1996, this FoodNet surveillance catchment area had an estimated population of 14,281,096 (5% of the US population). Based on the US Census Bureau's 1996 postcensal population estimates, the total infant population under surveillance during the study period was 194,256. Surveillance personnel from each FoodNet site contacted each of the clinical laboratories in the catchment area either weekly or monthly, depending on the size of the laboratory, for reports on culture-confirmed *Salmonella* cases in the catchment area.

Case-control study. In California, Connecticut, and Minnesota, the study was conducted between 1 May 1996 and 30 April 1997; in Georgia and Oregon, between 1 August 1996 and 31 July 1997. All patients aged <12 months who were infected with nontyphoidal *Salmonella* serogroups B or D were considered eligible for the case-control study, except in Minnesota during the last 11 months of the study, where 1 of every 3 patients was randomly selected to be eligible. This study focused on *Salmonella* serogroups B and D because, in 1996, they accounted for >60% of all reported *Salmonella* infections in the United States, including the 2 most frequent serotypes, Typhimurium and Enteritidis [19]. We obtained informed consent from participants and conducted this study in accordance with guidelines for human research specified by the US Department of Health and Human Services.

FoodNet personnel attempted to interview parents or guardians of all eligible patients within 21 days after a specimen was obtained. Parents or guardians of patients were not interviewed if any of the following criteria were met: the patient did not reside within the catchment area, the patient's parent or guardian could not be reached by phone, or the patient's parent or guardian was unable to answer questions (e.g., because the parents did not speak English). Patients whose parents or guardians were interviewed were excluded from the study if any of the following criteria were met: the interview was conducted 21 days after a specimen was obtained, the patient's parent or guardian was unable to give the date of onset of their infant's illness, the onset of illness was ⩾10 days before the date the specimen was obtained, the onset of illness occurred ⩽28 days after another culture-confirmed case of salmonellosis in the same household, the patient was part of a recognized outbreak in which the vehicle of transmission was clearly identified, or *Salmonella* of the same serotype had been previously isolated from the patient in the previous 12 months. During the interview, a standardized questionnaire was administered concerning demographic data, clinical course, preexisting illness, diet, prior antimicrobial use, food-handling techniques, and travel history in the 5 days before illness onset.

Attempts were made to match each case patient to 2 control subjects from the catchment area population according to age-specific strata (1–5 months and 6–11 months) and either vital record birth list or telephone exchange. In 4 FoodNet sites, control subjects were selected by random sampling from a zip code–specific vital record birth list. In the fifth FoodNet site (Georgia), control subjects were identified by sequential digit dialing based on the telephone exchange of the patient. Potential control subjects were excluded from enrollment if any of the following criteria were met: their primary residence was outside the catchment area, their parent or guardian was not English-speaking, they were ill within the 28 days before the matched case patient's date of illness onset, or their parent or guardian reported an occurrence of a culture-confirmed nontyphoidal serogroup B or D *Salmonella* infection within the 28 days before the matched case patient's date of illness onset. Failure to enroll an eligible control subject within 7 days of the matched case patient interview resulted in the exclusion of the case patient from the case-control study.

SAS software, version 6.12 (SAS), and LogXact software, version 2.1 (Cytel), were used for analysis [20, 21]. Race or ethnicity was categorized as white or nonwhite. Parent or guardian's highest level of education completed was categorized into 2 groups: at least some college education and no college education. Area of residence, as described by the respondent, was also categorized as urban/suburban or other town/village/rural (i.e., nonurban). Annual household income was categorized into the following strata: <$15,000; $15,000–$29,999; $30,000–$59,999; $60,000–$99,999; and ⩾$100,000. Birth weight was categorized as ⩽3.18 kg (the overall median birth weight) and >3.18 kg. For continuous data, mean values for case patients and control subjects were compared using Student's *t* test. Kaplan-Meier survival analysis was used to compare age at which breast-feeding was discontinued between case patients and control subjects who had ever been breast-fed. Fisher's exact test was used to compare proportions. For all statistical tests, a 2-

sided P value of ≤.05 was considered significant. For the multivariate analysis, a model was constructed incorporating a variable for breast-feeding, a factor known a priori to be inversely associated with infant salmonellosis, and all variables that were significantly associated with illness in univariate analysis. A single, ordinal variable representing the infant's liquid diet in the 5 days before illness onset was constructed with 3 levels. The 3 levels of this ordinal variable were: (1) liquid diet of breast milk only, including human milk fed to a child with a cup (referent level), (2) liquid diet of breast milk and either formula or water, and (3) liquid diet containing no breast milk. Exclusive breast-feeding was defined as breast-feeding, drinking no formula or water, and consuming no solid food in the 5 days before illness onset. Further analysis was conducted to assess potential interaction between the effect of breast-feeding and age and to calculate the population-attributable fractions [22] for factors significantly associated with infant salmonellosis. Ninety-five percent CIs were computed for model-adjusted exposure-specific attributable fractions using a jackknife procedure outlined by Kahn et al. [23].

RESULTS

Active surveillance. Two hundred sixty-one infant cases of culture-confirmed, nontyphoidal *Salmonella* infection were ascertained during the study period (134 cases/100,000 infants per year). Of the 261 infants with salmonellosis, 140 were infected with *Salmonella* serogroup B or D. Of the patients with serogroup B or D *Salmonella* infections for whom hospitalization data ($n = 138$) and outcome data ($n = 134$) were collected, 36 (26.1%) of 138 patients were hospitalized and 0 (0%) of 134 patients died. After excluding 19 cases in Minnesota due to the random selection process, 121 cases were eligible for the study.

Case-control study. Of the 121 eligible case patients, parents or guardians of 71 (59%) were interviewed. The primary reason for not being interviewed was that the patient's parent or guardian could not be contacted by phone. The mean age of these 71 patients who were interviewed was 6.1 months, and 44% were female. As a result of their illness, 23 (32%) of these patients were admitted to a hospital, and the average length of stay was 4 days. For 43% of the patients, a family member missed work because of the infant's illness (average number of days missed, 3.8). In addition to diarrhea, patients frequently reported the symptoms of fever (75% of patients), bloody diarrhea (61%), and loss of appetite (53%). Of the isolates collected for these 71 patients, 93% were from stool and 7% were from blood. The most common infecting *Salmonella* serotypes were Typhimurium (in 45% of patients) and Heidelberg (in 17%) (table 1).

Thirty-seven (52%) of the 71 case patients with interviews

Table 1. Clinical and demographic characteristics of patients included and patients with interviews but excluded from the FoodNet infant salmonellosis case-control study, 1996–1997.

Characteristic, by class	Patients included (n = 22)	Patients with interviews but excluded (n = 49)
Clinical		
Serogroup of isolates		
B	20 (91)	43 (88)
D	2 (9)	6 (12)
Serotype of isolates		
Agona	0 (0)	3 (6)
Enteritidis	1 (5)	5 (10)
Heidelberg	5 (22)	7 (15)
Saint Paul	2 (9)	3 (6)
Typhimurium	12 (55)	20 (41)
Other[a]	2 (9)	9 (18)
Unknown	0 (0)	2 (4)
Demographic		
Site of residence		
California	1 (5)	17 (35)
Connecticut	4 (18)	12 (24)
Georgia	7 (32)	14 (29)
Minnesota	6 (27)	2 (4)
Oregon	4 (18)	4 (8)
Sex		
Female	12 (55)	19 (39)
Male	10 (45)	30 (61)
Race or ethnicity		
White	13 (59)[b]	12 (24)[b]
Nonwhite	9 (41)	37 (76)
Parent's/guardian's education level		
No college	12 (55)	20 (41)
At least some college	10 (46)	23 (47)
Unknown	0 (0)	6 (12)
Area of residence		
Urban	15 (68)	30 (61)
Nonurban	7 (32)	19 (39)
Annual household income		
<$15,000	4 (18)	18 (37)
$15,000–$29,999	4 (18)	11 (23)
$30,000–$59,999	5 (23)	5 (10)
$60,000–$99,999	4 (18)	6 (12)
≥$100,000	0 (0)	2 (4)
Unknown	5 (23)	7 (14)
Medical insurance		
Any	19 (86)	45 (92)
None	1 (5)	2 (4)
Unknown	2 (9)	2 (4)
Mean age, months	5.8	6.2
Mean gestational age, weeks	36.0	38.2
Mean birth weight, kg	3.0	3.2

NOTE. Data are no. (%) of patients, unless otherwise indicated.

[a] Serotypes Derby, Durban, Java, Javiana, Paratyphi B, Schwarzengrund, and 4,5,12:i:-.

[b] $P = .01$ for comparison of the proportion of whites among the case patients included in the study and among those excluded.

were excluded from the study, which left 34 patients with interviews in the study. Reasons for exclusion included the following: the patient's parent or guardian was interviewed >21 days after the sample was collected (73% of patients), the patient's onset of illness was ⩾10 days before the sample was collected (14%), the patient's infection was related to a recognized outbreak in which the vehicle of transmission was clearly identified (9%), and *Salmonella* of the same serotype had been isolated from the patient in the past 12 months (4%). Either 1 or 2 control subjects were found for 22 (65%) of the remaining 34 patients with interviews. These 22 case patients were matched to 39 control subjects. Of those 22 case patients, 17 were matched to 2 control subjects and 5 were matched to 1 control subject. The 22 enrolled patients did not differ significantly from the 37 excluded patients or the 12 patients with interviews but without matched control subjects with respect to age, sex, annual household income, parent or guardian education level, or frequency distribution of isolates by *Salmonella* serotype (table 1). The enrolled group had a higher proportion of white patients than did the excluded group (59% vs. 24%; $P < .01$). The enrolled patient group and the excluded patients with interviews group did not differ with respect to proportion hospitalized, mean length of hospital stay, or proportion with bloody stool during illness. Furthermore, among the patients with interviews for whom breast-feeding information was available, the proportion who were breast-fed in the 5 days before illness onset did not differ significantly between the enrolled group (0 [0%] of 20) and the excluded group (3 [15%] of 20; $P = .23$).

In a univariate analysis of patient demographic characteristics, the 22 case patients and 39 matched control subjects did not differ significantly with respect to sex, race, residential area, annual household income, or medical insurance status (table 2). Reflecting the age-matching of control subjects to case patients, the ages of control subjects were within 80 days of the ages of matched case patients. Also, the gestational age at birth of case patients did not differ significantly from that of control subjects. However, having a birth weight of ⩽3.18 kg was a significant risk factor for salmonellosis: 17 (77%) of the 22 case patients had a birth weight of ⩽3.18 kg, compared with 18 (46%) of 39 control subjects ($P = .04$). Also, having a parent with at least some college education was a significant protective factor. Ten (45%) of the 22 case patients had a parent with at least some college education, compared with 29 (74%) of 39 control subjects ($P = .03$).

In a univariate analysis of exposures, salmonellosis was significantly associated with being in a household where a member had diarrhea in the 4 weeks before illness onset, drinking water in the 5 days before illness onset, and drinking commercial-brand formula in the 5 days before illness onset (table 3). The results of univariate analysis also suggest that case patients were more likely to have eaten solid food than were control subjects (matched OR [MOR], 4.7; $P = .06$). Breast-feeding during the 5 days before illness onset had a strong protective effect: 0 (0%) of 20 case patients were breast-fed during this 5-day period, compared with 19 (51%) of 37 control subjects (MOR, 0.05; $P < .01$) (table 3). When we stratified by age group, we found that the protective effect of breast-feeding within the 5 days

Table 2. Demographic characteristics of case patients and control subjects, univariate analysis, FoodNet infant salmonellosis case-control study, 1996–1997.

Characteristic	Case patients ($n = 22$)	Control subjects ($n = 39$)
Site of residence		
California	1 (5)	2 (5)
Connecticut	4 (18)	8 (21)
Georgia	7 (32)	9 (23)
Minnesota	6 (27)	12 (31)
Oregon	4 (18)	8 (21)
Sex		
Female	12 (55)	15 (41)
Male	10 (45)	24 (59)
Race or ethnicity		
White	13 (59)	26 (67)
Nonwhite	9 (41)	13 (33)
Parent's/guardian's education level		
No college	12 (55)	10 (26)
At least some college	10 (45)[a]	29 (74)[a]
Area of residence		
Urban	15 (68)	20 (51)
Nonurban	7 (32)	19 (49)
Annual household income		
<$15,000	4 (18)	7 (18)
$15,000–$29,999	4 (18)	5 (13)
$30,000–$59,999	5 (23)	13 (33)
$60,000–$99,999	4 (18)	5 (13)
⩾$100,000	0 (0)	5 (13)
Unknown	5 (23)	4 (10)
Medical insurance		
Any	19 (86)	38 (97)
None	1 (5)	1 (3)
Unknown	2 (9)	0 (0)
Birth weight of ⩽3.18 kg	17 (77)[b]	18 (46)[b]
Mean age, months	5.8	6.8
Mean gestational age, weeks	36.0	37.0

NOTE. Data are no. (%) of subjects, unless otherwise indicated.

[a] $P = .03$ for the comparison of the proportion of infants who had parents/guardians with at least some college education (case patients vs. control subjects).

[b] $P = .04$ for the comparison of the proportion of infants with birth weight of ⩽3.18 kg (case patients vs. control subjects).

Table 3. Distribution of selected risk factors among case patients and control subjects, univariate regression analysis, FoodNet infant salmonellosis case-control study, 1996–1997.

	Proportion (%) of subjects			
Risk factor	Case patients	Control subjects	MOR[a] (95% CI)	Exact *P*
Exposures[b]				
Water	22/22 (100)	31/39 (79)	8.66 (1.17–∞)	.03
Formula	19/20 (95)	23/35 (66)	7.77 (1.01–354.8)	.05
Any breast milk				
All infants	0/20 (0)	19/37 (51)	0.05 (0–0.30)	<.01
Infants aged <6 months	0/15 (0)	16/25 (64)	0.05 (0–0.33)	<.01
Infants aged 6–11 months	0/5 (0)	3/12 (25)	0.83 (0–10.65)	.89
Breast milk exclusively[c]				
All infants	0/22 (0)	2/38 (5)	0.56 (0–7.46)	.67
Infants aged <6 months	0/15 (0)	2/24 (8)	0.56 (0–7.46)	.67
Infants aged 6–11 months	0/7 (0)	0/14 (0)	…	…
Any solid food	16/20 (80)	20/35 (57)	4.70 (0.94–45.94)	.06
Eggs	1/17 (6)	2/35 (6)	2.00 (0.05–∞)	.67
Attended day care facility	3/21 (14)	7/39 (18)	0.77 (0.06–5.76)	1.0
Living on or visiting a farm	2/22 (9)	2/39 (5)	2.73 (0.12–176.8)	.81
Reptiles inside or outside the home	3/22 (14)	3/38 (8)	1.79 (0.23–13.53)	.75
Pets in the home	7/22 (32)	17/39 (44)	0.65 (0.18–2.10)	.60
Household member had diarrhea[d]	11/22 (50)	1/38 (3)	18.21 (2.61–789.1)	<.01

[a] Matched odds ratio; case patients and control subjects were matched by age and either telephone exchange or zip code–specific vital record birth list.
[b] For case patients, exposure during the 5 days before illness onset; for control subjects, 5 days before the date of illness onset in the matched case patient.
[c] Consumption of breast milk, no formula, no water, and no solid food.
[d] For case patients, during the 4 weeks before illness onset; for control subjects, during the 4 weeks before illness onset date in the matched case patient.

before illness onset was significant among infants <6 months of age (MOR, 0.05; $P < .01$) but not significant among infants aged ⩾6 months (MOR, 0.8; $P = .89$). Furthermore, among the 15 case patients and 33 control subjects who were ever breast-fed, case patients stopped breast-feeding at an earlier age than did control subjects (median age, 1.4 vs. 7.0 months; $P < .01$) (figure 1). Salmonellosis was not significantly associated with eating eggs, attending a day care facility, living on or visiting a farm, exposure to reptiles, or having pets in the household during the 5 days before illness onset.

In a multivariate analysis, after adjusting for birth weight of ⩽3.18 kg and for having a parent with at least some college education, salmonellosis was associated with drinking water or formula in the 5 days before illness onset and living in a household where a family member had recently had diarrhea (table 4). Considering the 5 days before illness onset and using a liquid diet of only breast milk as the referent exposure, we found that case patients were more likely than matched control subjects to have a liquid diet of breast milk and either water or formula (MOR, 6.7) and even more likely to have a liquid diet of no breast milk (MOR, 44.5; $P = .04$). Case patients were more likely to reside in a household where a member had diarrhea in the 4 weeks before illness onset (MOR, 13.2; $P = .01$). The population-attributable fraction for having a liquid diet other than only breast milk was 98% (95% CI, 74%–100%), and that for living in a household where a member recently had diarrhea was 43% (95% CI, 20%–66%).

DISCUSSION

Our study showed a strong association between having a liquid diet other than breast milk only and sporadic infant salmonellosis, which suggests that breast-feeding prevents infant salmonellosis. Biologic evidence supports the protective effect of breast milk. An in vitro study by France et al. [13] showed that phagocytic cells in colostrum and breast milk were active against *Salmonella*, indicating that breast milk can provide host defense for the breast-fed infant. Another possible explanation for the protective effect of breast-feeding is that other characteristics of the care or environment of breast-fed infants are different from those for non–breast-fed infants, so that exposure to *Salmonella* is less common among breast-fed infants.

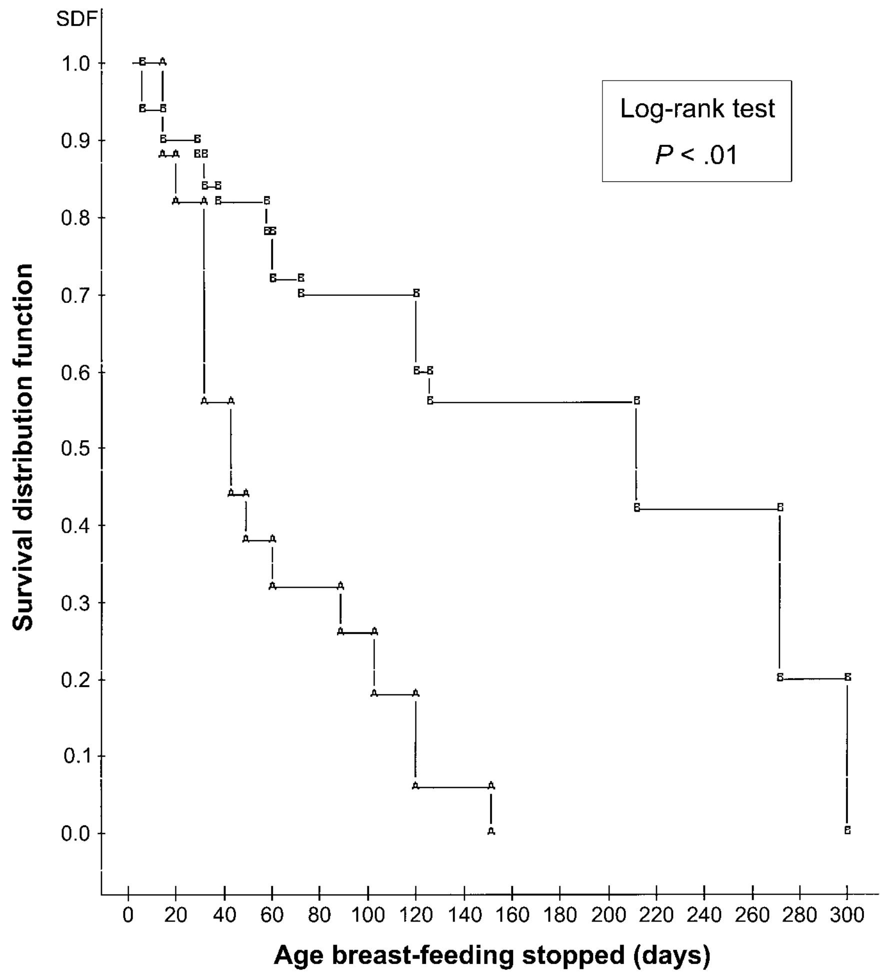

Figure 1. Age of discontinuation of breast-feeding among infants who had ever been breast-fed for 15 case patients *(A)* and 33 control subjects *(B)* in the FoodNet infant salmonellosis case-control study, 1996–1997.

For example, non–breast-fed infants drink formula or water, and, during the course of feeding or preparation, infant formula or water can become contaminated with *Salmonella.* Infant formula has been shown to support the growth of *Salmonella* [24]. If formula is contaminated during preparation and then kept warm for several hours, bacterial growth is highly likely. This scenario has been well documented as a source of *Yersinia enterocolitica* infections in bottle-fed infants who were cared for by persons who simultaneously were preparing raw pork tripe [25].

However, after adjusting for characteristics such as being in a household where a member recently had diarrhea and having a parent or guardian with at least some college education, breast-feeding remained protective. The protective effect of breast-feeding in our study also is unlikely to result from confounding due to child's age, since control subjects were age-matched with case patients. Furthermore, in our study, the protective effect of breast-feeding was only statistically significant for infants <6 months of age; and, among infants who had ever been breast-fed, case patients stopped breast-feeding at a younger age than control subjects. These findings support the current recommendations for infants to be breast-fed through infancy and to be fed breast milk exclusively for the first 6 months of life [26].

Our study suggests that 74%–100% of the risk for infant salmonellosis could be eliminated if infants drank breast milk and no formula and no water. The applicability of this estimated reduction in risk relies heavily on the assumption that we obtained an unbiased sample of case patients in the population. In our study, no case patients were breast-fed in the 5 days before illness onset; this might be an underestimation of the true proportion of case patients in the population exposed to breast milk in the 5 days before illness onset. The component of the population-attributable fraction that estimates the case patients' exposure percentage could therefore be high, causing an artificially inflated estimate of attribution.

In 1995, a national mail survey found that 60% of postpartum women were breast-feeding at the time of hospital dis-

Table 4. Results of multivariate regression analysis, FoodNet infant salmonellosis case-control study, 1996–1997.

Risk factor	AOR[a] (95% CI)	Exact *P*
Liquid diet (breast milk/formula/water)[b]	6.67 (1.07–∞)	.04
Household member had diarrhea[c]	13.16 (1.77–∞)	.01
Birth weight of ≤3.18 kg	3.18 (0.33–∞)	.33
Parent/guardian with at least some college education	1.00 (0–39.0)	1.0

[a] Adjusted matched odds ratio; case patients and control subjects matched by age and either telephone exchange or zip code–specific vital record birth list.

[b] Ordinal variable with 3 levels: (1) liquid diet of breast milk only (referent level), (2) liquid diet of breast milk and either formula or water, and (3) liquid diet containing no breast milk.

[c] For case patients, during the 4 weeks before illness onset; for control subjects, during the 4 weeks before the date of illness onset in the matched case patient.

charge, and 22% were still breast-feeding 6 months later [27]. Motivated by the strong epidemiologic evidence that breast-feeding and human milk decreases an infant's risk for a large number of acute and chronic diseases, the Healthy People 2000 National Health Promotion and Disease Prevention Objectives called for an increase in the nationwide prevalence of breast-feeding at the time of hospital discharge and 6 months later to 75% and 50%, respectively [28]. Our study findings suggest that an increase in the prevalence of breast-feeding is likely to also lead to a decrease in the incidence of infant salmonellosis.

In our study, living in a household where a member recently had diarrhea was also associated with salmonellosis. This finding indicates the possibility of person-to-person transmission of *Salmonella,* either directly or by contaminated food or formula. Furthermore, approximately one-half of isolates in our study were *S.* Typhimurium. In a study of children aged <4 years old (one-half of whom were aged <1 year), the PFGE patterns of *S.* Typhimurium isolates from index patients matched PFGE patterns of isolates from ill farm animals, household members, vacuum cleaners, and household dirt associated with the index patients [18]. The role of the infant's home environment is difficult to discern in such studies because transmission may have occurred from the environment to the infant or vice versa. Nevertheless, the study suggested that contaminated food might not be a common direct source of *Salmonella* for infants [18]. To prevent indirect transmission, caretakers of infants need to be reminded about the importance of washing their hands before they handle their infants or prepare food or drink for their infants, particularly if they themselves have had a diarrheal illness.

This study has several important limitations. First, our study had a low response rate: only 22 (18.2%) of 121 eligible case patients were enrolled. Selection bias might be present if the reasons that eligible case patients were excluded from the study were associated with exposure factors and infant salmonellosis. For example, a source of possible selection bias was that a greater proportion of enrolled case patients were of white race, and white persons generally are more likely to practice breast-feeding [27]. However, in our study, none of the enrolled white case patients were breast-fed in the 5 days before illness onset. Another potential source of selection bias was that we only included case patients who had a home phone number. Lacking a home phone number might indicate low socioeconomic status, a characteristic that has been shown to be associated with low likelihood of breast-feeding [27] and increased risk of salmonellosis [13]. In our study, however, a relatively small percentage of eligible case patients were excluded because they lacked a home phone number. Another source of selection bias was that this study included only persons who spoke English. Since we did not interview any non–English-speaking persons about their health outcomes or history of exposures, we do not know the magnitude of the bias caused by requiring English speaking in our selection of study participants. Other findings might reduce the likelihood of selection bias. For example, case patients who were identified by FoodNet and whose parents or guardians were interviewed but who were not included in the case-control study did not differ from case patients who were included in the study with respect to age, sex, annual household income, parent or guardian education level, or frequency distribution of isolates by *Salmonella* serotype. In addition, among case patients for whom breast-feeding information was available, the proportion of infants who were breast-fed within the 5 days before illness onset among case patients who were excluded from the study was not different from the proportion among case patients who were included. Thus, we believe the strong protective effect of breast-feeding is not likely to have resulted solely from bias due to our selection of case patients.

Other study limitations included a small sample size and the exclusion of patients with infections due to *Salmonella* belonging to serogroups other than B or D. A small sample size might have reduced the statistical power to detect significant differences in frequencies of factors between case patients and control subjects. For example, our study did not find statistically significant associations between infant salmonellosis and risk factors for salmonellosis commonly found among older children and adults, such as eating foods of animal origin (e.g., eggs), recent reptile or pet exposure, living on or visiting a farm, or travel outside of the United States [7–11]. However, in our study, MORs were >1.0 for eating solid food, living on or visiting a farm, and exposure to reptiles; thus, exposure-associated risk should be further explored in larger studies. Furthermore, the lack of association between reptile exposure and infant salmonellosis could have resulted from our inclusion of only patients with serogroup B or D *Salmonella* infections;

reptiles are a reservoir for a broad range of *Salmonella* serotypes [29].

Another limitation of the study was our dependence on parental recall for infants' illness characteristics and exposures. Recall bias might be introduced if parents of ill infants remembered their infants' exposure and food history differently from parents of healthy infants. This study attempted to reduce recall bias by conducting case patient interviews within 21 days after the date the specimen was obtained, conducting control subject interviews within 7 days after the case patient interviews, and asking control subjects about exposures within a window of time comparable to that for case patients. Indeed, in our efforts to reduce recall bias, we excluded a large proportion of eligible case patients, which resulted in a decreased sample size.

CONCLUSIONS

In summary, our study findings indicate a strong protective effect of breast-feeding against nontyphoidal, sporadic serogroup B and D *Salmonella* infection for infants residing in the FoodNet catchment area. Results from our population-based study and similar results from other studies of different study populations and methodologies provide a substantial body of evidence for the benefits of breast-feeding. Not only could increased breast-feeding decrease the burden of *Salmonella* infection among infants, but also it could reduce health care costs and parental absenteeism from work that are attributable to the infant's illness. Pediatric health care providers and community education programs should encourage mothers to breast-feed when appropriate, provide caretakers of infants with information about salmonellosis, and give advice about hand washing and safe preparation of formula and solid food for infants.

FOODNET WORKING GROUP MEMBERS

CDC: Frederick Angulo, Thomas Boyce, Mary Evans, Patricia Griffin, Sudha Reddy, David Swerdlow, Robert Tauxe, Drew Voetsch, and Samantha Yang Rowe. California: Felicia Chi, Pam Daily, Kevin Reilly, Art Reingold, Gretchen Rothrock, Sue Shallow, Duc Vugia, Stephen Waterman, and Ben Werner. Georgia: Molly Bardsley, Wendy Baughman, Paul Blake, Shama Desai, Monica Farley, Jane Koehler, Suzanne Segler, and Kathleen Toomey. Connecticut: Terry Rabatsky-Ehr, James Hadler, Ruthanne Marcus, Pat Mshar, and Robin Ryder. Minnesota: Jeff Bender, Valerie Deneen, Craig Hedberg, Julie Hogan, Heidi Kassenborg, and Michael Osterholm. Oregon: Maureen Cassidy, Paul Cieslak, David Fleming, Theresa McGivern, Beletshachew Shiferaw, Regina Stanton, and John Townes. Maryland: Diane Dwyer and Peggy Pass. New York: Hwa-Gan Chang, Julia Kiehlbauch, Dale Morse, and Cathy Stone. US Department of Agriculture/Food Safety Inspection Service: Art Baker, Jill Hollingsworth, Peggy Nunnery, Phyllis Sparling, and Kaye Wachsmuth. US Food and Drug Administration: Sean Alterkruse, Ken Falci, and Bing Garthwright.

Acknowledgment

We are grateful to the public health officers at the California, Connecticut, Georgia, Minnesota, and Oregon FoodNet sites for their efforts to contact infants' parents and administer questionnaires. We also thank Dr. Robert M. Hoekstra and Dr. Frederick J. Angulo for their editorial contributions.

References

1. Mead PS, Slutsker L, Dietz V, et al. Food-related illness and death in the United States. Emerging Infect Dis **1999**; 5:607–25.
2. Frenzen PD, Riggs TL, Buzby JC, et al. *Salmonella* cost estimate updated using FoodNet data. Food Review **1999**; 22:10–5.
3. Cohen ML, Tauxe RV. Drug-resistant *Salmonella* in the United States: an epidemiologic perspective. Science **1986**; 234:964–9.
4. Hohmann EL. Nontyphoidal salmonellosis. Clin Infect Dis **2001**; 32: 263–9.
5. Stutman HR. *Salmonella, Shigella,* and *Campylobacter:* common causes of infectious diarrhea. Pediatr Ann **1994**; 23:538–43.
6. Centers for Disease Control and Prevention (CDC). 1996 Final FoodNet surveillance report. Atlanta: CDC, **1998**.
7. Tauxe RV. *Salmonella:* a postmodern pathogen. J Food Prot **1991**; 54: 563–8.
8. Salmonellosis associated with chicks and ducklings—Michigan and Missouri, spring 1999. MMWR Morb Mortal Wkly Rep **2000**; 49: 297–9.
9. Mermin J, Hoar B, Angulo FJ. Iguanas and *Salmonella marina* infection in children: a reflection of the increasing incidence of reptile-associated salmonellosis in the United States. Pediatrics **1997**; 99:399–402.
10. Kass PH, Farver TB, Beaumont JJ, et al. Disease determinants of sporadic salmonellosis in four northern California counties: a case-control study of older children and adults. Ann Epidemol **1992**; 2:683–96.
11. Delarocque-Astagneau E, Desenclos JC, Bouvet P, Grimont PA. Risk factors for the occurrence of sporadic *Salmonella enterica* serotype Enteritidis infections in children in France: a national case-control study. Epidemiol Infect **1998**; 121:561–7.
12. Blake PA, Ramos S, MacDonald KL, et al. Pathogen-specific risk factors and protective factors for acute diarrheal disease in urban Brazilian infants. J Infect Dis **1993**; 167:627–32.
13. France GL, Marmer DJ, Steele RW. Breast-feeding and *Salmonella* infection. Am J Dis Child **1980**; 134:147–52.
14. Borgnolo G, Barbone F, Scornavacca G, et al. A case-control study of *Salmonella* gastrointestinal infection of Italian children. Acta Paediatr **1996**; 85:804–8.
15. Raisler J, Alexander C, O'Campo P. Breast-feeding and infant illness: a dose-response relationship? Am J Public Health **1999**; 89:25–9.
16. Haddock RL, Malilay J. A search for infant salmonellosis risk factors on Guam. Southeast Asian J Trop Med Public Health **1984**; 17:38–42.
17. Haddock RL, Nocon FA. Infant salmonellosis and vacuum cleaners. J Trop Pediatr **1994**; 40:53–4.
18. Schutze GE, Sikes JD, Stefanova R, Cave MD. The home environment and salmonellosis in children. Pediatrics **1999**; 103:E1.
19. US Department of Health and Human Services (DHHS). Centers for Disease Control and Prevention. *Salmonella* annual tabulation summary 1996. DHHS Publication PHS 733-001/80527. Atlanta: Government Printing Office, **1999**.

20. SAS [computer program]. Version 6.12 for Windows. Cary, NC: SAS Institute, **1989–1996**.
21. Cytel Software Corporation. LogXact [computer program]. Version 2.1 for Windows. Cambridge, MA: Cytel Software, **1992–1997**.
22. Bruzzi P, Green SB, Byar DP, et al. Estimating the population attributable fraction for multiple risk factors using case-control data. Am J Epidemiol **1985**; 122:904–14.
23. Kahn MJ, O'Fallon WM, Sicks JD. General population attributable risk estimation. Technical report 54. Rochester, MN: Mayo Clinic, revised July **2000**.
24. Usera MA, Rodriguez A, Echeita A, Cano R. Multiple analysis of a foodborne outbreak caused by infant formula contaminated by an atypical *Salmonella* Virchow strain. Eur J Clin Microbiol Infect Dis **1998**; 17:551–5.
25. Lee LA, Taylor J, Carter GP, et al. *Yersinia enterocolitica* O:3: an emerging cause of pediatric gastroenteritis in the United States. J Infect Dis **1991**; 163:660–3.
26. Working Group on Breastfeeding. Breastfeeding and the use of human milk. Pediatrics **1997**; 100:1035–9.
27. Ryan AS. The resurgence of breastfeeding in the United States. Pediatrics **1997**; 99:E12. Available at: http://www.pediatrics.org/cgi/content/full/99/4/e12. Accessed on 16 March 2004.
28. US Department of Health and Human Services (DHHS). Healthy people 2000: national health promotion and disease prevention objectives. DHHS Publication PHS 91–502212. Washington, DC: Government Printing Office, **1990**.
29. Burnham BR, Atchley DH, DeFusco RP, et al. Prevalence of fecal shedding of *Salmonella* organisms among captive green iguanas and potential public health implications. J Am Vet Med Assoc **1998**; 213:48–50.